Patent claims

1. Biocompatible material comprising a substratum contacted by at least one macromolecule,

said material having a first advancing contact angle a in the range of from 60 to 125 degrees,

said substratum having a second advancing contact angle b_0 when not contacted by a macromolecule, and another second advancing contact angle b_{sat}, when said substratum is saturated by said macromolecules,

wherein said advancing contact angles are measured using water and air saturated by water vapour,

wherein b_{sat} essentially does not change when the substratum is contacted by further macromolecules by means of a chemical bond,

wherein the relation between said advancing contact angles is as defined by the ratio R,

$$R = (b_0 - a) / (b_0 - b_{sat})$$

and wherein the numerical value of R is in the interval from and including 0 to less than 0.4.

2. Material according to claim 1, wherein said substratum comprises a hydrophobic polymer.

3. Material according to claim 2, wherein said substratum has an advancing contact angle of more than 90 degrees.

4. Material according to any of claims 1 to 3, wherein said macromolecule comprises an amphiphilic polymer.

Replacement sheet - Rule 66.8 PCT

80

5. Material according to claim 1, wherein the substratum is further contacted by a plurality of soluble substances capable of forming a self-assembled monolayer comprising at least one macromolecule.

6. Material according to claim 5, wherein said soluble substances are n-alkane chains preferably containing from 8 to 24 carbons.

7. Material according to any of claims 1 to 6, wherein said substratum is pretreated or modified, preferably by contacting the substratum with a charged group or a hydrophilic compound.

8. Material according to claim 1, wherein said first advancing contact angle is in the range of from 70 degrees to 120 degrees.

9. Material according to claim 8, wherein said first advancing contact angle is in the range of from 75 degrees to 110 degrees.

10. Material according to claim 8, wherein said first advancing contact angle is in the range of from 80 degrees to 100 degrees.

11. Material according to any of claims 1 to 4, wherein said ratio is in the range of from 0 to less than 0.30.

12. Material according to claim 11, wherein said ratio is in the range of from 0 to less than 0.20.

13. Material according to claim 11, wherein said ratio is in the range of from 0 to less than 0.10.

14. Material according to claim 11, wherein said ratio is in the range of from 0 to less than 0.05.

15. Material according to any of claims 1 to 4, wherein the first advancing contact angle a is substantially identical to the advancing contact angle b_0.

Replacement sheet - Rule 66.8 PCT

81

16. Material according to any of the preceding claims, wherein said material, when contacted by a first determinant comprising a compound selected from the group consisting of a polypeptide, or part thereof, a nucleic acid moiety, a carbohydrate moiety, and a lipid moiety, including any combination thereof, is capable of maintaining said compound in a biologically active form.

17. Material according to claim 16 wherein said compound is a polypeptide or part thereof.

18. Material according to claim 16 or 17 further comprising said first determinant comprising said compound, wherein said first determinant is maintained in a biologically active form when contacted by said substratum and/or said macromolecule.

19. Material according to claim 18 wherein said biologically active form is essentially a biologically active conformation.

20. Material according to any of claims 15 to 19 wherein said biologically active form or conformation is maintained and/or improved and/or stabilized by means of the cooperativity of said substratum and said macromolecule.

21. Material according to claim 15 to 19 wherein said biologically active form or confirmation is maintained and/or improved and/or stabilized when contacted by said substratum and said macromolecule.

22. Material according to any of the preceding claims, wherein the weight increase per area unit arising from the part of the macromolecule essentially consisting of PEG or poly(ethylene oxide) (PEO) is less than 2.0×10^{-22} grams (g) per square nanometer (nm^2).

23. Material according to claim 22, wherein said difference is less than 0.3×10^{-22} grams (g) per square nanometer (nm^2).

24. Material according to any of claims 1 to 23, wherein said substratum is at least substantially flexible.

25. Material according to claim 24, wherein said substratum is a film.

26. Material according to any of claims 1 to 23, wherein said substratum is essentially rigid or at least substantially non-flexible.

27. Material according to claim 26, wherein said substratum comprises a crystalline structure capable of supporting a self-assembled monolayer such as gold, silicon oxide, and similar crystalline structures and/or structures that are smooth on a nanometer scale.

28. Material according to any of the preceding claims, wherein said macromolecule has a MW of more than 400 Da.

29. Material according to claim 28, wherein said macromolecule has a MW of more than 5.000 Da.

30. Material according to claim 28, wherein said macromolecule has a MW of more than 10.000 Da.

31. Material according to any of the preceding claims, wherein said macromolecule is a conjugate comprising a head group, a guiding group, a linker group, a polymer chain or a main body, and a functional end group.

32. Material according to claim 31, wherein said head group is capable of adsorbing onto the substratum.

33. Material according to claim 32, wherein said head group is capable of forming an ionic bond.

34. Material according to claim 32, wherein said head group is capable of forming a self-assembled monolayer.

35. Material according to claim 32, wherein said head group is capable of forming a chemical bond.

36. Material according to claim 32, wherein said head group is entangled into or with the substratum.

37. Material according to claim 31, wherein said guiding group is a bifunctional group comprising an aliphatic, linear or weakly branched group.

38. Material according to claim 31, wherein said linker group is capable of being enzymatically or chemically hydrolyzed.

39. Material according to claim 31, wherein said linker group is essentially stable against cleavage under practical circumstances.

40. Material according to claim 31, wherein said polymer chain or main body is preferably hydrophilic, uncoiling in an aqueous environment and exhibiting an excluded volume.

41. Material according to claim 31, wherein said functional end group is capable of linking permanently or reversibly other biological or synthetic molecules or materials.

42. Material according to any of claims 16 to 21, wherein said biologically active compound is selected from the group consisting of membrane associated and/or extracellular matrix polypeptides natively produced by a microbial cell, a plant cell or a mammalian cell.

43. Material according to claim 42 wherein said biologically active compound is selected from the group consisting of a polypeptide, an antibody, a polyclonal antibody, a monoclonal antibody, an immunogenic determinant, an antigenic determinant, a receptor, a receptor binding protein, an interleukine, a cytokine, a cellular differentiation factor, a cellular growth factor, and an antagonist to a receptor.

44. Material according to claim 42, wherein said biologically active compound is a synthetic polypeptide, or part thereof, capable of contacting said substratum and/or said macromolecule.

45. Material according to claim 42, wherein said biologically active compound is a synthetic polypeptide, or part thereof, capable of contacting said substratum and said macromolecule.

46. Material according to claim 42, wherein said biologically active compound is an adhesion polypeptide, preferably fibronectin or vitronectin.

47. Material according to any of claims 42, wherein said biologically active compound results in an improved contact between said material and a biological entity, such as a biological cell or a virus, or part thereof, including a polypeptide, or a part thereof, a nucleic acid moiety, a carbohydrate moiety, and a lipid moiety, including any combination thereof.

48. Material according to any of the preceding claims, said material further comprising a second determinant.

49. Material according to claim 48, wherein said second determinant comprises a biological entity, such as a biological cell or a virus, or part thereof, including a polypeptide, or a part thereof, a nucleic acid moiety, a carbohydrate moiety, and a lipid moiety, including any combination thereof.

50. Material according to claim 49, wherein said biological entity is selected from the group consisting of a polypeptide, an antibody, a polyclonal antibody, a monoclonal antibody, an immunogenic determinant, an antigenic determinant, a receptor, a receptor binding protein, an interleukine, a cytokine, a differentiation factor, a growth factor, and an antagonist to the receptor.

51. Material according to claim 49, wherein said biological cell, or part thereof, is selected from the group consisting of a mammalian cell, including a human cell and an animal cell, a plant cell, a microbial cell, including a eukaryotic microbial

cell, including a yeast and a fungus, and a prokaryotic microbial cell including a bacteria.

52. Material according to claim 51 wherein said biological cell is a mammalian cell.

53. Material according to any of the preceding claims, wherein said substratum is porous and preferably a membrane.

54. Material according to claim 53, wherein the flux of water through said material is substantially unchanged as compared to the flux of water through said porous substratum.

55. Material according to any of claims 1 to 52, wherein said substratum is non-porous and/or substantially non-penetrable to water.

56. Material according to any of the preceding claims for use in a method of controlling cellular growth and/or cellular proliferation and/or cellular differentiation ex vivo.

57. Material according to any of the preceding claims for use in a method of separating and/or isolating biological material ex vivo.

58. Material according to any of claims 1 to 55 for use in a diagnostic method carried out on the human or animal body.

59. Material according to any of claims 1 to 55 for use in a method of therapy carried out on the human or animal body.

60. Material according to any of claims 1 to 55 for use in a method of surgery carried out on the human or animal body.

61. Material according to any of claims 1 to 55 for use as a carrier for in vivo delivery of a medicament to a human or animal body in need of said medicament.

Replacement sheet - Rule 66.8 PCT

86

62. Pharmaceutical composition comprising the material according to any of claims 1 to 55 and a pharmaceutically active ingredient and optionally a pharmaceutically active carrier.

63. Use of the material according to any of claims 1 to 55 or the pharmaceutical composition according to claim 62 in a method of controlling cellular growth and/or cellular proliferation and/or cellular differentiation ex vivo.

64. Use of the material according to any of claims 1 to 55 or the pharmaceutical composition according to claim 62 in a method of separating and/or isolating biological material ex vivo.

65. Use of the material according to any of claims 1 to 55 or the pharmaceutical composition according to claim 62 in a method of producing a biohybrid organ ex vivo.

66. Method of controlling cellular growth and/or cellular proliferation and/or cellular differentiation ex vivo, said method comprising the steps of contacting a cell with the material according to any of claims 1 to 55, or the pharmaceutical composition according to claim 62, and incubating said cell and said material under conditions allowing said cell to grow and/or proliferate and/or differentiate.

67. Method of separating and/or isolating biological material ex vivo, said method comprising the steps of contacting said biological material to be separated and/or isolated with the material according to any of claims 1 to 55, or the pharmaceutical composition according to claim 62, and incubating said biological material and said material under conditions that allow separation and/or isolation.

68. Method of producing a biohybrid organ ex vivo, said method comprising the steps of contacting biohybrid organ cells with the material according to any of claims 1 to 55, or the pharmaceutical composition according to claim 62, and incubating said biohybrid organ cells under conditions allowing the production of said biohybrid organ.

69. Method of in vivo delivery of a medicament to a human or animal body in need of said medicament, said method comprising the steps of contacting said body with the pharmaceutical composition according to claim 62 and incubating said body contacted by said pharmaceutical composition under conditions allowing delivery of said medicament.

70. Method for producing the material according to any of claims 1 to 55, said method comprising the steps of i) providing a substratum having a second advancing contact angle, and ii) contacting said substratum with a composition comprising a plurality of macromolecules.

71. Method according to claim 70, wherein said substratum comprises a hydrophobic polymer.

72. Method according to claim 70, wherein said substratum is pretreated prior to being contacted by said macromolecule.

73. Method according to claim 70, wherein said pretreatment is effective in increasing the wettability of said substratum.

74. Method according to claim 70, wherein said macromolecule comprises a hydrophilic polymer.

75. Method according to claim 70, wherein said macromolecule comprises a latently reactive polymer.

76. Method according to claim 70, wherein macromolecule has a MW of more than 400 Da.

77. Method according to claim 70, wherein said macromolecule comprises a conjugate comprising a cross likable head group, a linker group, a polymer chain, and a functional end group.

78. Method according to claim 77, wherein said cross linkable head group is a photo-reactive aryl azide head group.

Replacement sheet - Rule 66.8 PCT

88

79. Method according to claim 77, wherein said macromolecule further comprises a modifying agent.

80. Method according to claim 79 wherein said modifying agent is capable of contacting said substratum and forming a self assembled monolayer.

81. Method according to any of claims 70 to 80 for producing the material according to any of claims 1 to 55, said method comprising the further step of contacting said material with a first determinant comprising a biologically active compound.

82. Method according to claim 81, wherein said biologically active compound is selected from the group consisting of a polypeptide, an antibody, a polyclonal antibody, a monoclonal antibody, an immunogenic determinant, an antigenic determinant, a receptor, a receptor binding protein, an interleukine, a cytokine, a cellular differentiation factor, a cellular growth factor, and an antagonist to a receptor.

83. Method according to claim 81, wherein said biologically active compound is a membrane associated and/or extracellular matrix polypeptide natively produced by a microbial cell, a plant cell or a mammalian cell.

84. Method according to any of claims 81 to 83 for producing the material according to any of claims 1 to 55, said method comprising the further step of contacting said material with a second determinant comprising a biological entity.

85. Method according to claim 84, wherein said biological entity comprises a cell or a virus, or a part thereof.

86. Method according to claim 85, wherein said cell, or part thereof, is selected from the group consisting of a mammalian cell, including a human cell and an animal cell, a plant cell, a microbial cell, including a eukaryotic microbial cell, including a yeast and a fungus, and a prokaryotic microbial cell including a bacteria.

87. Method according to claim 85, wherein said virus, or part thereof, is selected from a mammalian virus, including a human virus and an animal virus, a plant virus, a microbial virus, including a eukaryotic microbial virus, including a yeast virus and a fungal virus, and a prokaryotic microbial virus including a bacteriophage.

88. Method according to claim 84, wherein said biological entity comprises a polypeptide, or a part thereof, a nucleic acid moiety, a carbohydrate molety, and a lipid molety, including any combination thereof.

89. Method according to claim 84, wherein said biological entity is selected from the group consisting of a polypeptide, an antibody, a polyclonal antibody, a monoclonal antibody, an immunogenic determinant, an antigenic determinant, a receptor, a receptor binding protein, an interleukine, a cytokine, a differentiation factor, a growth factor, and an antagonist to the receptor.